REMARKS

Claims 1, 4-8, 11, 14, 19-21, 24, 28-30 and 35-37 are currently pending. Claims 2-3, 9-10, 12-13, 15-18, 22-23, 25-27, and 31-34 have been canceled. Claims 1, 14 and 24 are currently amended. Claims 38-40 are new. Support for the claim amendments and new claims may be found throughout the specification and claims as published (U.S. Publication No. 2004/0259101), for example, at least at paragraphs [007], [0013], [0027], [0034], and Examples 1-3. Applicant believes that no new matter is presented by the amendment.

Amendment of the originally filed claims, or cancellation of any claims should in no way be construed as an acquiescence, narrowing, or surrender of any subject matter. The amendments are being made not only to point out with particularity and to claim the present invention, but also to expedite prosecution of the present application.

Rejections under 35 U.S.C. § 112, First Paragraph

The Office rejected claims 14, 19-21, 24, 28-30 and 36-37 under 35 U.S.C. § 112, first paragraph alleging failure to comply with the enablement requirement. In particular, the Office states, on page 4 of the instant Action, that the method is not enabled "because it has not been shown that just any 'positive' result from just any additional assay indicates that a patient has cancer, precancer, or has abnormal proliferating colorectal cancer cells." Applicant respectfully traverses the rejection.

Without acquiescing to the Office's position, Applicant has amended independent claim 14 to recite "performing at least one additional assay to detect at least one marker indicative of colorectal cancer or precancer on a stool sample from the patient identified as a positive screen to determine if the patient has abnormal proliferating colorectal cancer cells." Claims 19-21 and 36 depend from claim 14. Also, without acquiescing to the Office's position, Applicant has amended claim 24 to recite "performing at least one additional assay to detect at least one marker indicative of colorectal cancer or precancer to determine if the patient has colorectal cancer or precancer." Claims 28-30 and 37 depend from claim 24. Applicant believes that the amendment to claims 14 and 24 obviates the rejection. Accordingly, Applicant respectfully requests withdrawal of this rejection.

Rejections under 35 U.S.C. § 103

The Office rejected claims 1, 4, 7, 11 and 35 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Loktionov *et al.* (Clinical Research, 1998, 4:337-342) in view of Hromadnikova *et al.* (BMC Pregnancy and Childbirth, 2002, 2:1-5). Applicant respectfully traverses the rejection.

Without acquiescing to the rejection, Applicant has amended claim 1 to recite "wherein the quantitative amount of genome equivalents is determined by measuring an amount of nucleic acid fragments amplified from shed cells and shed cellular debris." As acknowledged by the Office, "Loktionov et al. determines [an] amount of amplified 113 bp fragments of patient genomic DNA using a subpopulation of a stool sample" (see page 13, underlining added). As previously asserted by Applicant, Loktionov *et al.* does not disclose measuring genomic DNA from a stool sample comprising shed cells and shed cellular debris, where such DNA may be substantially degraded. Rather, Loktionov *et al.* teach measuring an amount of DNA extracted from whole cells. Specifically, Loktionov *et al.* teach isolating exfoliated colonocytes using magnetic beads coated with epithelium-specific antibodies and washing the whole cells before cell lysis, DNA extraction, and quantitation. Because Loktionov's method isolates whole cells prior to cell lysis it selects only a subpopulation of the DNA that is present in the stool sample. As such, Loktionov's method does not isolate shed cellular debris that is naturally present in the stool sample. Therefore, Loktionov's method cannot be used for determining a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells and shed cellular debris as recited in amended claim 1 because Loktionov does not disclose or suggest isolating DNA from shed cellular debris in a stool sample.

Hromadnikova *et al.* does not cure the deficiencies of Loktionov. As acknowledged by the Office, Hromadnikova does not teach or suggest a method of determining a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells and cellular debris (see page 15 of the Office action). Since neither Loktionov nor Hromadnikova, alone or in combination, teach or suggest the claimed invention, Applicant respectfully requests withdrawal of the rejection.

The Office rejected claims 1, 4-8, 11, 14, 19-21, 24, 28-30 and 35-37 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Loktionov *et al.* (Clinical Research, 1998, 4:337-342) in view of Hromadnikova *et al.* (BMC Pregnancy and Childbirth, 2002, 2:1-5) and further in view of Ahlquist *et al.* (Gastroenterology, 2000, 119:1219-1227). Applicant respectfully traverses the rejection.

Without acquiescing to the rejection, Applicants have amended claims 1, 14 and 24 to recite "wherein the quantitative amount of genome equivalents is determined by measuring an amount of nucleic acid fragments amplified from shed cells and shed cellular debris." Claims 4-8, 11 and 35 depend from claim 1; claims 19-21, and 36 depend from claim 14; and claims 28-30 and 37 depend from claim 24. As discussed above neither Loktionov nor Hromadnikova teach or suggest "determining a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells and shed cellular debris, wherein the quantitative amount of genome equivalents is determined by measuring an amount of nucleic acid fragments amplified from shed cells and shed cellular debris," as required by claims 1, 14, and 24. Ahlquist does not cure the deficiencies of Loktionov and Hromadnikova. Consequently, the combination of references, *i.e.*, Loktionov, Hromadnikova, and Ahlquist fails to teach or suggest the claimed subject matter taken as a whole as required by 35 U.S.C. § 103. Therefore, Applicant respectfully requests that the rejection be withdrawn.

The Office has further rejected claims 1, 4-8, 11, 14, 19-21, 24, 28-30 and 35-37 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Lapidus et al. (U.S. Patent No. 6,143,529) in view of Hromadnikova et al. (BMC Pregnancy and Childbirth, 2002, 2:1-5). Applicant respectfully traverses the rejection.

Without acquiescing to the rejection, Applicant has amended claims 1, 14 and 24 to recite that "the amount of genome equivalents is above a predetermined threshold amount of genome equivalents, wherein the predetermined threshold amount comprises at least 10 genome equivalents." None of the cited references teach or suggest a threshold amount of at least 10 genome equivalents for determining (i) whether a patient is a candidate for additional cancer testing, (ii) whether the patient has abnormal proliferating cancer cells, or (iii) whether the patient has colorectal cancer or precancer as recited in amended claims 1, 14 and 24. In contrast,

the instant application has determined threshold amounts of DNA for accurately discriminating healthy patients from cancer patients requiring additional cancer testing. In view of the foregoing, Applicants respectfully submit that neither Lapidus nor Hromadnikova, alone or in combination, teach or suggest the claimed subject matter taken as a whole as required by 35 U.S.C. § 103.

CONCLUSION

Applicant respectfully requests reconsideration of the rejections and allowance of the pending claims in due course. The Examiner is cordially invited to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance, or if there are any questions regarding this case.

Respectfully submitted,

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